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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,181	08/02/2006	Stefan Evers	21729	8450

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
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EXAMINER	
GITOMER, RALPH J	
ART UNIT	**PAPER NUMBER**
1657	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,181	EVERS ET AL.	
	Examiner	Art Unit	
	Ralph Gitomer	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/9/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The RCE Request received 5/28/08 and the IDS received 6/9/08 have been entered and claims 21 and 23 are considered here. Claims 27-37 are listed as withdrawn, however in view of the final Office Action of 1/11/08 they are presumed to have been canceled because claims 27-37 are drawn to an invention nonelected with traverse in the reply filed on 5/22/07.

It would appear the point of novelty is screening for specific inhibitors of PDE4D isotypes of PDE4 to identify inhibitors that will treat atherosclerosis or restenosis. It was known to do the same with PDE4 which may have been a mixture of isotypes, so a specific inhibitor for PDE4D only would be presumed to have greater treatment specificity assuming the inhibitor effectively inhibited only PDE4D or its subtypes and not PDE4 in general. However, this has not been taught by the specification as originally presented nor claimed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Arguments have been presented regarding enabling issues in the disclosure of the cited reference. Neither the present specification nor claims state any degree of specificity regarding the compound identified to inhibit the stated isotypes of PDE4. And no compounds are disclosed that are specific inhibitors. On page 8 Figs. 5 and 6 are directed to determining rolipram and cilomilast inhibition of PDE4D, both well known PDE4 inhibitors that also inhibit PDE4D. On page 16 an assay is shown for PDE4D with rolipram but no data is presented. No other inhibitors are screened or identified, only those two known inhibitors and no specificity from PDE4 to PDE4D is seen. Therefor no correlation is seen between identifying a compound that inhibits atherosclerosis or restenosis and the compound specifically inhibiting PDE4D or other subtypes versus merely inhibiting PDE4 in general. No inhibitor specificity for any isoform of PDE4 is seen nor any data regarding this issue presented. No new inhbitors of PDE4 are disclosed or identified, only known inhibitors.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frenette.

Frenette (WO 00/64874) entitled "Heterosubstituted Pyridine Derivatives as PDE4 Inhibitors" teaches on page 2, the finding of multiple PDE4's raises the prospect of obtaining inhibitors that are selective for individual isoforms, thus increasing the specificity of action of such inhibitors. The cDNA's of each of A, B, C and D isoforms have been reported. Many of the PDE4 inhibitors which have been synthesized have lacked selectivity and are reported to be emetic such as rolipram. On page 2 last line rolipram is a known PDE4 inhibitor. On page 11 line 22 treating arterial restenosis and atherosclerosis particularly is taught.

The claims differ from Frenette in that they are directed to screening and identifying modulators of isotypes of PDE4 such as PDE4D.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to screen and identify inhibitors of PDE4D in view of the teachings of Frenette because Frenette teaches "obtaining" inhibitors for specific known isoforms of PDE4 in order to avoid the problems with non-specific inhibitors of PDE4. And these inhibitors would be employed to treat arterial restenosis and atherosclerosis.

Applicant's arguments filed 5/28/08 have been fully considered but they are not persuasive.

Applicants argue that Frenette does not disclose activity of PDE4 as related to atherosclerosis or stenosis nor enable their treatment with a compound that is an inhibitor of PDE4. And Frenette does not disclose administering a compound suspected to be an activator or inhibitor of PDE4 to the PDE4 target. Specific isoforms of PDE4 are not suggested as a treatment target.

It is the examiner's position that Frenette teaches on page 11 line 22, PDE4 inhibitors are useful to treat arterial restenosis and atherosclerosis, which is at least an invitation to try. The document shows a number of protocols and examples to determine the activity of inhibitors of PDE4, see page 40 for a screening assay where IC50 values are determined. No specificity is claimed for specific isoforms of PDE4 where rolipram would be expected to inhibit all of them. The importance of inhibitor specificity is well known in this art and is discussed in Frenette.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

The preamble of claim 21 is directed to screening but lacks any such step. The newly added limitation to claim 21(a) regarding the target is an isoform of PDE4 makes the rest of the claim inconsistent where in 21(c) and 23 it may be intended to be "of the PDE4 target" in all occurrences to have proper antecedent basis. In claim 21(b) it is unclear why the compound may be suspected to be an activator if in the last step the compound is an inhibitor. It is noted no specificity is claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ralph Gitomer/
Primary Examiner, Art Unit 1657

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